Attachment C. Recommendations Regarding Investigator Responsibilities

The HHS 45 CFR 46 Regulation for the Protection of Human Subjects in Research, unlike FDA regulations (312 and 812), does not directly address the roles and responsibilities of investigators involved in human subjects research. Investigators are in the best position to protect participants.

In the recent report "MORAL SCIENCE: Protecting Participants in Human Subjects Research," the Presidential Commission for the Study of Bioethical Issues recommended that "The Common Rule should be revised to include a section directly addressing the responsibilities of investigators. Doing so would bring it into harmony with the Food and Drug Administration regulations for clinical research and international standards that make the obligations of individual researchers more explicit, and contribute to building a stronger culture of responsibility among investigators." We agree that encouraging a culture of responsibility among investigators is an important goal of human subject protection regulations and the addition of investigator responsibilities to the regulations would be an important step in fostering this culture.

SACHRP proposes the addition to 45 CFR 46 of three sections that would cover, at a minimum: (1) responsibilities of investigators; (2) qualification standards for investigators (e.g., training); and (3) investigator documentation/records.

New regulations to ensure investigator accountability would codify the current ethical expectations for investigators who conduct research involving human subjects. Regulations addressing investigator responsibility should emphasize the critical role of the investigator and hold the investigator directly accountable for his/her actions.

Adding investigator responsibilities to the HHS regulations would harmonize HHS regulations with those of the FDA and international standards, uniting the regulatory expectations. Models for delineating investigator responsibilities can be found in the drug and device regulations of the FDA (i.e., Subpart D, 21 CFR Part 312 and Subpart E, 21 CFR Part 812) and in internationally accepted guidelines such as the ICH standards (Good Clinical Practice E-6, Section 4) and the CIOMS International Ethical Guidelines For Biomedical Research.

Therefore, SACHRP recommends the following language for inclusion in 45 CFR 46:

§46.102 (to be added to definitions)

> *Investigator means any individual responsible for the conduct of research involving human subjects, either for the study as a whole or for an individual site. If the research is conducted by a team at a study site, the investigator is the responsible leader of the team. The responsible person may also be called the principal investigator.*

§46.104 Responsibilities of Investigators.

(a) As appropriate to their role in the research, investigators are responsible for ensuring that research is conducted according to:

(1) sound research design and methods;

(2) the IRB approved study plan (protocol);

(3) the applicable terms of the grant, contract and/or signed funding agreements;

(4) applicable laws and regulations, including those for protecting the rights, safety, and welfare of human subjects.

(b) Investigators are responsible for ensuring that members of the research team, including study staff and trainees, are appropriately qualified, trained and supervised

(b) Unless exempt from review, investigators are responsible for obtaining initial IRB approval, prior approval for any modifications to the research and, as required, continuing review of the research.

(c) Investigators are responsible for providing the IRB with sufficient information and materials to make the required determinations in §46.111.

(d) Unless waived by the IRB, investigators are responsible for ensuring that informed consent is obtained in accordance with §46.116 and as approved by the IRB.

(e) Unless waived by the IRB, investigators are responsible for ensuring consent is documented to the extent required by §46.117 and as approved by the IRB.

(f) Investigators are responsible for providing a copy of the informed consent document to each subject, unless the requirement of a written consent document is not part of the IRB approval.

(g) Investigators are responsible for providing subjects with significant new findings developed during the course of the research that may relate to their willingness to continue participation, in accordance with §46.116.

(h) When vulnerable populations are involved in research, investigators are responsible for implementing any additional safeguards as required by the IRB.

(i) Investigators are required to permit and facilitate monitoring and auditing, at reasonable times, by the IRB of record, funding entities, sponsors, the Secretary, and other federal and state regulatory agencies, as appropriate.

(j) Investigators shall ensure prompt reporting to the IRB of any noncompliance with the approved protocol or requirements of the IRB, and unanticipated problems involving risks to subjects or others.

(k) Investigators are responsible for personally conducting or supervising the research.

(m) Investigators are responsible for complying with regulatory and institutional requirements, including those relating to financial interests, which are relevant to the research.

§46.105 Qualification Standards for Investigators.

(a) As appropriate to their role in the research, investigators must be sufficiently qualified by education, training, and experience to assume responsibility for the proper conduct of the research.

(b) Investigators must assure that they have sufficient time and resources to properly conduct or supervise the research for which they are responsible.

§46.106 Investigator Records, Reports and Documentation.

(a) Investigators are responsible for the safe and secure storage of research data (whether in paper or electronic formats) and for protecting the confidentiality of the data in accordance with the approved protocol.

(b) Investigators are responsible for the accuracy and completeness of study data.

(c) Investigators must maintain records appropriate to the research (e.g., the study plan, consent forms, and correspondence from the IRB) and permit inspection of the research records in accordance with §46.104(j).

(d) Investigators must maintain records for at least three years after the research ends or for the length of time specified in applicable regulations or applicable institutional or sponsor requirements, whichever is longer, and should take measures to prevent accidental or premature destruction of these documents.

(e) Investigators must submit written reports to the IRB as required by the IRB.